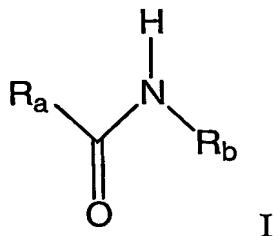


What is claimed is:

1. A composition for prophylaxis or treatment of viral infections, said composition comprising a therapeutically effective amount of a compound, including pharmaceutically acceptable salts thereof, selected from the group of those having the formulas:

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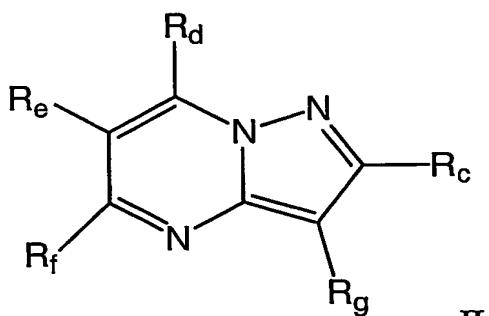
wherein:

10  $R_a$  represents a radical selected from the group consisting of cycloalkyl, a heterocyclic radical, a substituted or unsubstituted aryl group, and a substituted or unsubstituted heteroaryl group;

$R_b$  represents a radical selected from the group consisting of a substituted or unsubstituted aryl group and a substituted or unsubstituted heteroaryl group;

15 said aryl group substituents and said heteroaryl group substituents being one or more radical(s) independently selected from the group consisting of alkyl, alkoxy, halogen, phenylamido, a heterocyclic radical, and a substituted or unsubstituted heterocyclosulfonyl;

said heterocyclosulfonyl substituents being one or more radical(s) independently selected from the group consisting of a heteroaryl group;



20

wherein  $R_c$  represents a radical selected from the group consisting of a substituted or unsubstituted aryl group and  $-C(=O)NH-R_h$ ;

$R_d$  represents a radical selected from the group consisting of hydroxy and polyhaloalkyl;

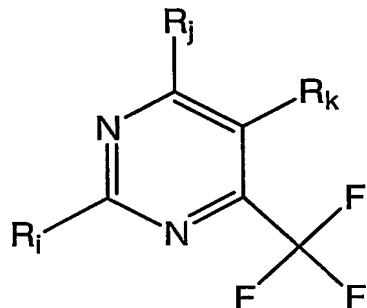
$R_e$  represents a radical selected from the group consisting of hydrogen, alkyl, alkenyl, and arylalkyl;

5  $R_f$  represents a radical selected from the group consisting of alkyl, phenyl and a heteroaryl group;

$R_g$  represents a radical selected from the group consisting of hydrogen and alkyl;

$R_h$  represents a radical selected from the group consisting of cycloalkyl, arylalkyl, and heteroarylalkyl;

10 said aryl group substituents being one or more radical(s) independently selected from the group consisting of alkyl, alkoxy, and halogen;



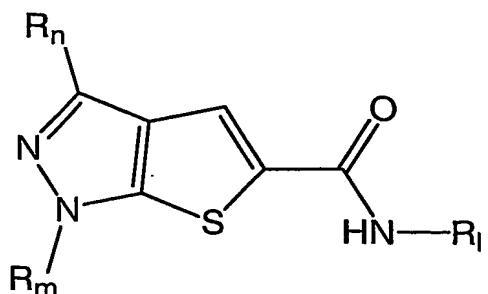
III

15 wherein  $R_i$  represents a radical selected from the group consisting of amino, hydroxy, and a substituted or unsubstituted heterocyclic radical;

$R_j$  represents a radical selected from the group consisting of a substituted or unsubstituted aryl;

20  $R_k$  represents a radical selected from the group consisting of hydrogen, alkyl, a substituted or unsubstituted aryl, and a substituted or unsubstituted heteroaryl;

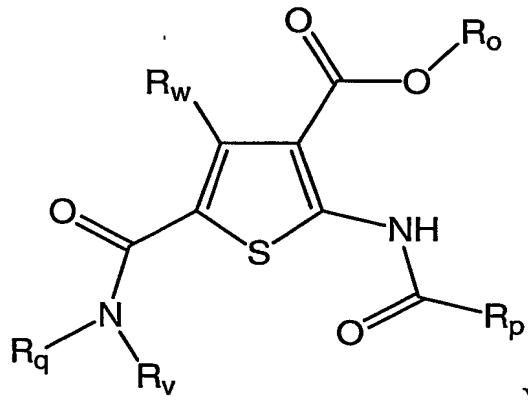
said aryl group substituents, said heterocyclic radical substituents, and said heteroaryl group substituents being one or more radical(s) independently selected from the group consisting of alkyl, alkoxy, and halogen;



IV

wherein R<sub>l</sub> and R<sub>m</sub> represent radicals that are independently selected from the group consisting of a substituted or unsubstituted aryl group and a substituted or unsubstituted heteroaryl group;

5 and R<sub>n</sub> represents a radical selected from the group consisting of an alkyl group; said aryl group substituents and said heteroaryl group substituents being one or more radical(s) independently selected from the group consisting of alkyl, alkoxy, halogen;



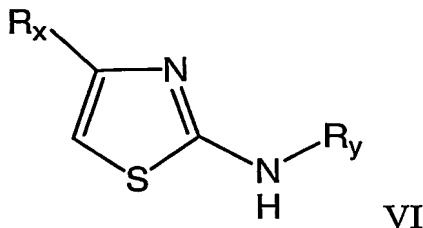
V

wherein R<sub>0</sub> represents a radical selected from the group consisting of an alkyl group; 10 R<sub>p</sub> represents a radical selected from the group consisting of alkyl, aralkyl,

heteroaralkyl, a bicyclic heterocycle, a substituted or unsubstituted aryl group, a substituted or unsubstituted heteroaryl group, and a substituted or unsubstituted aryloxyalkyl group;

R<sub>q</sub> represents a radical selected from the group consisting of alkyl, cycloalkyl, and a substituted or unsubstituted aryl group;

15 R<sub>v</sub> represents a radical selected from the group consisting of hydrogen and alkyl; R<sub>w</sub> represents a radical selected from the group consisting of an alkyl group; said aryl group substituents, said heteroaryl group substituents, and said aryloxyalkyl group substituents being one or more radical(s) independently selected from the group consisting of alkyl, alkoxy, and halogen;

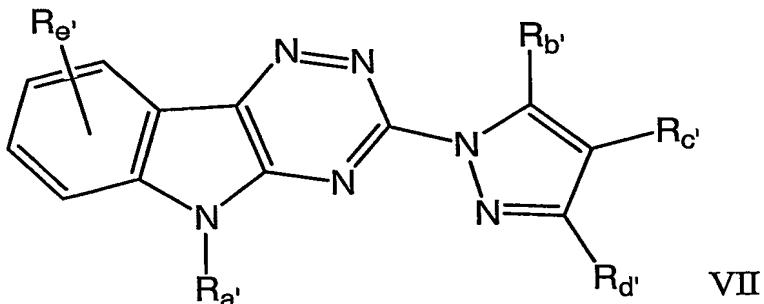


wherein  $R_x$  represents a radical selected from the group consisting of a substituted or unsubstituted aryl group and a substituted or unsubstituted heteroaryl group;

5       $R_y$  is selected from the group consisting of a substituted or unsubstituted aryl group and a substituted or unsubstituted heteroaryl group;

    said aryl group substituents and said heteroaryl group substituents being one or more radical(s) independently selected from the group consisting of alkyl, alkoxy, halogen, carboxyl, amino, amido, alkylcarbonyl, alkoxycarbonyl, and  $-\text{SO}_2\text{-(NH)-R}_z$ ; and

10      $R_z$  represents a radical selected from the group consisting of hydrogen and a heteroaryl group;



wherein:

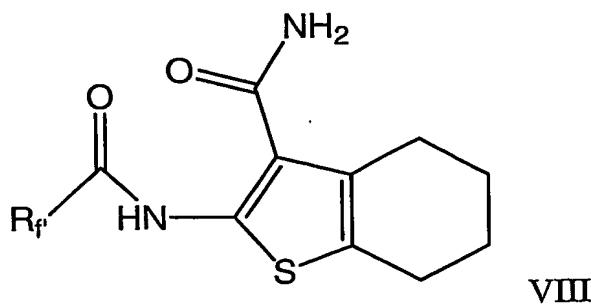
15      $R_{a'}$  represents a radical selected from the group consisting of hydrogen, alkyl, hydroxyalkyl, alkoxyalkyl, alkylthioalkyl, and dialkylaminoalkyl;

$R_{b'}$  represents a radical selected from the group consisting of hydrogen, alkyl, alkoxy, hydroxyalkyl, aryl, and heteroaryl;

20      $R_{c'}$  represents a radical selected from the group consisting of hydrogen, alkyl, alkoxy, hydroxyalkyl, aryl, and heteroaryl;

$R_{d'}$  represents a radical selected from the group consisting of hydrogen, alkyl, alkoxy, hydroxyalkyl, aryl, and heteroaryl; and

$R_{e'}$  represents a radical selected from the group consisting of alkyl, alkoxy, halogen, monoalkylamino, dialkylamino, and heteroaryl;



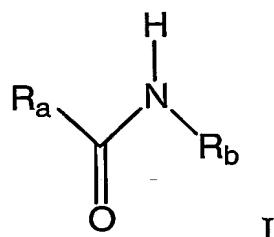
wherein

5         $R_f$  is selected from the group consisting of alkoxy, benzyl, and a substituted or unsubstituted phenyl;

      said phenyl group substituents being one or more radical(s) independently selected from the group consisting of alkyl, alkoxy, and halogen;  
and a pharmaceutically acceptable carrier medium.

10        2. A composition according to claim 1 further comprising at least one supplemental agent selected from the group of interferon, pegylated interferon, ribavirin, protease inhibitors, polymerase inhibitors, small interfering RNA compounds, anti-sense compounds, nucleotide analogs, nucleoside analogs, immunoglobulins, immunomodulators, hepatoprotectants, anti-inflammatory agents, antibiotics, antivirals, and anti-infective compounds.

15        3. A method for prophylaxis or treatment of hepatitis C infections and diseases associated with such infections in a living host having said infections, said method comprising administering to said living host a therapeutically effective amount of at least one compound having the formulas:



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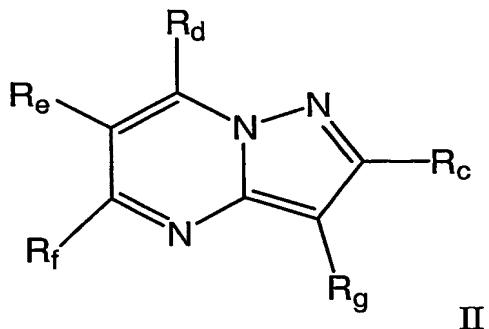
wherein:

$R_a$  represents a radical selected from the group consisting of cycloalkyl, a heterocyclic radical, a substituted or unsubstituted aryl group, and a substituted or unsubstituted heteroaryl group;

$R_b$  represents a radical selected from the group consisting of a substituted or unsubstituted aryl group and a substituted or unsubstituted heteroaryl group;

5        said aryl group substituents and said heteroaryl group substituents being one or more radical(s) independently selected from the group consisting of alkyl, alkoxy, halogen, phenylamido, a heterocyclic radical, and a substituted or unsubstituted heterocyclosulfonyl;        said heterocyclosulfonyl substituents being one or more radical(s) independently selected from the group consisting of a heteroaryl group;

10        and pharmaceutical salts thereof;



15        wherein  $R_c$  represents a radical selected from the group consisting of a substituted or unsubstituted aryl group and  $-C(=O)NH-R_h$ ;

$R_d$  represents a radical selected from the group consisting of hydroxy and polyhaloalkyl;

20         $R_e$  represents a radical selected from the group consisting of hydrogen, alkyl, alkenyl, and arylalkyl;

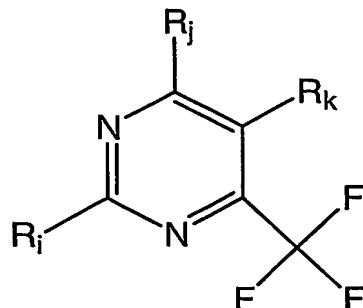
$R_f$  represents a radical selected from the group consisting of alkyl, phenyl and a heteroaryl group;

$R_g$  represents a radical selected from the group consisting of hydrogen and alkyl;

25         $R_h$  represents a radical selected from the group consisting of cycloalkyl, arylalkyl, and heteroarylalkyl;

      said aryl group substituents being one or more radical(s) independently selected from the group consisting of alkyl, alkoxy, and halogen;

and pharmaceutical salts thereof;



III

5 wherein R<sub>i</sub> represents a radical selected from the group consisting of amino, hydroxy, and a substituted or unsubstituted heterocyclic radical;

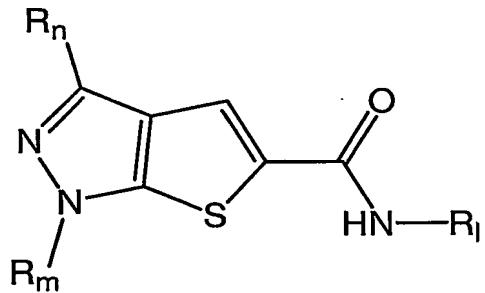
R<sub>j</sub> represents a radical selected from the group consisting of a substituted or unsubstituted aryl;

10 R<sub>k</sub> represents a radical selected from the group consisting of hydrogen, alkyl, a substituted or unsubstituted aryl, and a substituted or unsubstituted heteroaryl;

said aryl group substituents, said heterocyclic radical substituents, and said heteroaryl group substituents being one or more radical(s) independently selected from the group consisting of alkyl, alkoxy, and halogen;

and pharmaceutical salts thereof;

15

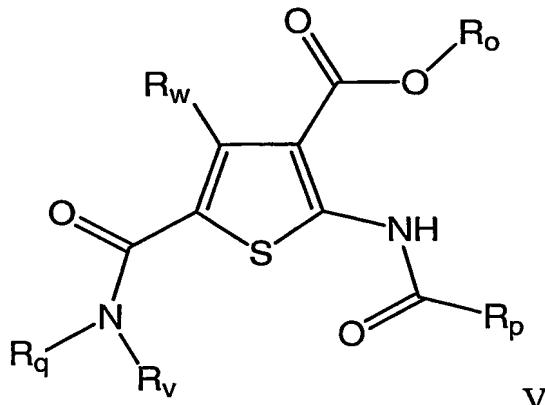


IV

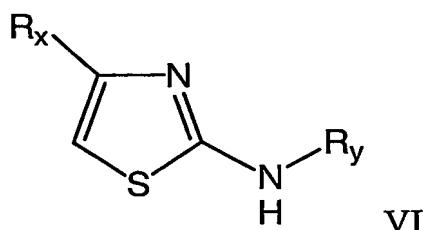
wherein R<sub>1</sub> and R<sub>m</sub> represent radicals that are independently selected from the group consisting of a substituted or unsubstituted aryl group and a substituted or unsubstituted heteroaryl group;

20 and R<sub>n</sub> represents a radical selected from the group consisting of an alkyl group;

said aryl group substituents and said heteroaryl group substituents being one or more radical(s) independently selected from the group consisting of alkyl, alkoxy, halogen; and pharmaceutical salts thereof;



5       wherein  $R_o$  represents a radical selected from the group consisting of an alkyl group;  
 $R_p$  represents a radical selected from the group consisting of alkyl, aralkyl, heteroaralkyl, a bicyclic heterocycle, a substituted or unsubstituted aryl group, a substituted or unsubstituted heteroaryl group, and a substituted or unsubstituted aryloxyalkyl group;  
10       $R_q$  represents a radical selected from the group consisting of alkyl, cycloalkyl, and a substituted or unsubstituted aryl group;  
 $R_v$  represents a radical selected from the group consisting of hydrogen and alkyl;  
 $R_w$  represents a radical selected from the group consisting of an alkyl group;  
      said aryl group substituents, said heteroaryl group substituents, and said aryloxyalkyl group substituents being one or more radical(s) independently selected from the group  
15      consisting of alkyl, alkoxy, and halogen;  
      and pharmaceutical salts thereof;



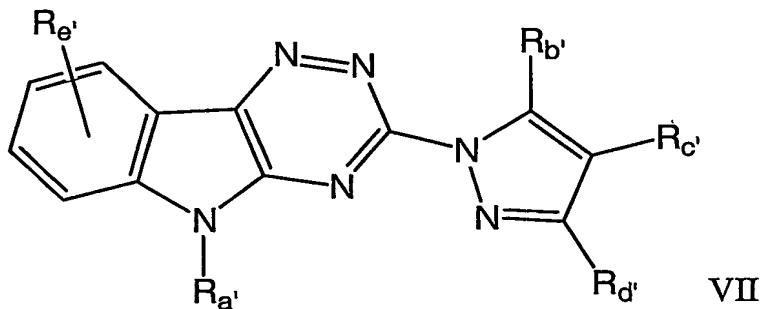
wherein  $R_x$  represents a radical selected from the group consisting of a substituted or  
20    unsubstituted aryl group and a substituted or unsubstituted heteroaryl group;  
       $R_y$  is selected from the group consisting of a substituted or unsubstituted aryl group and a substituted or unsubstituted heteroaryl group;

said aryl group substituents and said heteroaryl group substituents being one or more radical(s) independently selected from the group consisting of alkyl, alkoxy, halogen, carboxyl, amino, amido, alkylcarbonyl, alkoxy carbonyl, and  $-\text{SO}_2\text{-(NH)-R}_2$ ; and

$\text{R}_2$  represents a radical selected from the group consisting of hydrogen and a

5 heteroaryl group;

and pharmaceutical salts thereof;



10 wherein:

$\text{R}_a'$  represents a radical selected from the group consisting of hydrogen, alkyl, hydroxyalkyl, alkoxyalkyl, alkylthioalkyl, and dialkylaminoalkyl;

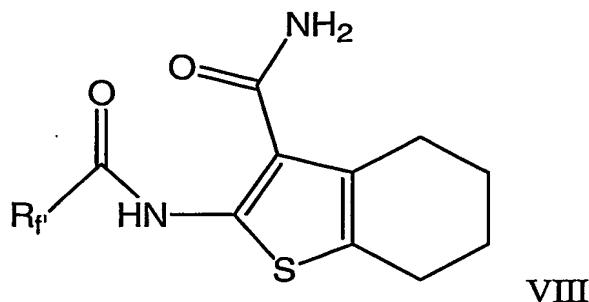
$\text{R}_b'$  represents a radical selected from the group consisting of hydrogen, alkyl, alkoxy, hydroxyalkyl, aryl, and heteroaryl;

15  $\text{R}_c'$  represents a radical selected from the group consisting of hydrogen, alkyl, alkoxy, hydroxyalkyl, aryl, and heteroaryl;

$\text{R}_d'$  represents a radical selected from the group consisting of hydrogen, alkyl, alkoxy, hydroxyalkyl, aryl, and heteroaryl; and

20  $\text{R}_e'$  represents a radical selected from the group consisting of alkyl, alkoxy, halogen, monoalkylamino, dialkylamino, and heteroaryl;

and pharmaceutical salts thereof; and



wherein

5       $R_f$  is selected from the group consisting of alkoxy, benzyl, and a substituted or unsubstituted phenyl;  
 said phenyl group substituents being one or more radical(s) independently selected from the group consisting of alkyl, alkoxy, and halogen;  
 and pharmaceutical salts thereof.

4. The method according to claim 3, wherein said living host is a mammal.
- 10     5. The method according to claim 3, wherein said living host is a human.
6. The method according to claim 3, wherein the compound is administered orally.
7. The method according to claim 3, wherein the compound is administered orally at a dose range of about 0.05 to about 100 mg/kg.
- 15     8. The method according to claim 3, wherein the compound is administered from 1 to 4 times daily.
9. The method according to claim 3, wherein the compound is administered in combination, either concurrently or sequentially, with at least one other biologically active agent.
- 20     10. The method according to claim 9, wherein said other biologically active agent is selected from the group consisting of interferon, pegylated interferon, ribavirin, protease inhibitors, polymerase inhibitors, small interfering RNA compounds, anti-sense compounds, nucleotide analogs, nucleoside analogs, immunoglobulins, immunomodulators,

hepatoprotectants, anti-inflammatory agents, antibiotics, antivirals, and anti-infective compounds.

11. A method for preventing apoptosis in a target cell comprising administration of an  
5 effective amount of NS4B to said cell.

12. A method for identifying compounds which modulate NS4B signal transduction comprising:

- 10 a) providing cells comprising an HCV replicon which express NS4B and exhibit reduced apoptosis;
- b) culturing the cells of step a) in the presence and absence of a test compound; and
- c) determining whether said compound alters NS4B associated apoptosis relative to untreated cells, thereby identifying a compound effective to inhibit NS4B signal  
15 transduction.

13. The method of claim 12, wherein NS4B signal transduction modulates a pathway selected from the group consisting of the interferon signaling pathway, the endoplasmic reticulum stress response pathway, the RNase L pathway, the 2'5' oligoadenylate pathway  
20 and the NF $\kappa$ b pathway.

14. The method of claim 12, wherein said compound inhibits NS4B signal transduction.

15. The method of claim 12, wherein said compound stimulates NS4B signal transduction.  
25

16. A method for identifying compounds which modulate NS4B-associated apoptotic inhibitory activity, comprising:

- 30 a) providing a host cell wherein NS4B is expressed;
- b) contacting said host cell with a test compound suspected of modulating NS4B associated apoptotic activity;
- c) assessing said modulation as a function of alterations in apoptosis levels in the presence of said agent.

17. A kit for practicing the method of claim 16, comprising host cells expressing NS4B, means for determining apoptosis of said cells, and instructional material.

18. A method for identifying compounds having binding affinity for NS4B comprising:

5           a) providing NS4B protein which is naturally fluorescent;

              b) contacting said NS4B protein with an agent suspected of having binding affinity for said NS4B;

              c) determining the fluorescence level of said NS4B in the presence and absence of said test compound, those agents which diminish the natural fluorescence of

10           NS4B having binding affinity for NS4B.

19. A compound having NS4B signal transducing inhibitory activity, said compound being effective to induce apoptosis in NS4B expressing cells which exhibit reduced apoptosis in the absence of said compound, said activity being determined by an NS4B binding assay method

15           comprising said compound in the presence of NS4B and determining the binding constant for said compound.

20. A compound according to claim 19, wherein the NS4B is an HCV protein.

20           21. A method for identifying compounds which modulate HCV NS4B signal transduction comprising:

              (a) testing a compound in HCV replicon assay and

              (b) testing said compound in HCV protein binding assays

25           22. A method of distinguishing NS4B biological activity from cellular chemical cytotoxicity for a test compound comprising: (a) measuring the apparent cytotoxicity of a compound in a host cell system, (b) measuring chemical cytotoxicity said compound in said host cell system containing NS4B protein, (c) comparing the results, and (d) identifying the apparent cytotoxicity as corresponding to NS4B biological activity or chemical cytotoxicity.

30           23. A method of treating an HCV infection in a patient in need of such treatment, said method comprising administering to said patient a pharmaceutically acceptable amount of compound that interacts with NS4B.

24. A method according to claim 23 wherein the said treatment results in modulation of cellular apoptosis.
- 5 25. A method according to claim 23 wherein said compound has HCV replicon activity.
26. A method according to claim 23 wherein said compound is identified using an HCV replicon assay and an NS4B binding assay.
- 10 27. A method according to claim 23, wherein said compound is administered with at least one agent selected from the group consisting of interferon, a pegylated interferon, ribavirin, a hepatoprotectant, acyclovir, famiclycolvir, valgancyclovir, and amantadine.
- 15 28. A compound having NS4B signal transducing inhibitory activity, said compound being effective to induce apoptosis in NS4B expressing cells which exhibit reduced apoptosis in the absence of said compound, said activity being determined by an assay method comprising contacting cells comprising an HCV replicon with said compound and analyzing said cells for apoptosis, said compound inhibiting NS4B signal transduction thereby stimulating apoptosis relative to cells not contacted with said compound.
- 20 29. The compound of claim 28, wherein said apoptosis is assessed via a method selected from the group consisting of measurement of DNA integrity, TUNEL assay, and trypan blue exclusion assay.
- 25 30. A compound having NS4B inhibitory activity but not having NS4B signal transducing inhibitory activity, said NS4B inhibitory activity being determined by an assay method comprising contacting cells comprising an HCV replicon with said compound, measuring viral replication, and analyzing said compound for NS4B binding activity.
- 30 31. A method for inducing apoptosis of hepatitis C-infected cells in a patient, said method comprising administering to said patient a compound of formula VII of claim 1 in an amount effective for induction of apoptosis of hepatitis C-infected cells in said patient, the induction of apoptosis being effected without producing toxemia in said patient.

32. The method of claim 31, wherein said compound is administered during the acute or silent phase of said infection.